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Attorney Docket No. 19374-504

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT(S): Farmer  
ASSIGNEE: Ganeden Biotech, Inc.  
SERIAL NUMBER: 09/369,016 EXAMINER: I. Marx  
FILING DATE: August 5, 1999 ART UNIT: 1651  
FOR: METHODS FOR INCREASING THE SOLUBILITY OF ESSENTIAL VITAMINS & MINERALS IN MAMMALS USING PROBIOTIC LACTIC ACID-PRODUCING BACTERIA, SYSTEMS, AND COMPOSITIONS

Cleveland, OH

Assistant Commissioner for Patents  
Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. § 1.132

I, John R. Fisgus, M.D., hereby declare and state as follows:

1. I am employed by MetroHealth Medical Center, Cleveland, Ohio. My title is Director of Obstetrical Anesthesia. I received an M.D. ~~in 1976~~ from the University of Buffalo, School of Medicine, in 1982. I am the Medical Advisor and Research Coordinator for Ganeden Biotech, Inc., the assignee of this application.

2. I am aware of the Examiner's November 5, 2002 Final Office Action. In particular, I understand that the Examiner contends that the methods and compositions of the present application are obvious over the teachings of Hata (U.S. Patent No. 4,210,672) taken with Paul (U.S. Patent No. 5,531,989) and Hansen (U.S. Patent No. 5,449,523) and further taken with Long (U.S. Patent No. 4,179,335) and the ATCC Catalogue of Bacteria ("ATCC"). Specifically, the Examiner asserts that "Applicants invention is predicated on an unexpected result, highly dependent upon specific proportions and/or amounts of particular ingredients. Any mixture of the components embraced by the claims which does not exhibit an unexpected result is therefore *ipso facto* unpatentable." (Final Office Action mailed November 5, 2002, paragraph bridging pages 3 and 4).

3. Digestion of lactose influences the bioavailability of minerals in milk. Lactose intolerant individuals have an inadequate supply of the enzyme lactase, which is required for the

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digestion of lactose. Lactose intolerance is evaluated by detection of gastrointestinal symptoms resulting from the incomplete digestion of lactose, the carbohydrate in cow's milk. Symptoms include abdominal pain, flatulence, bloating, cramps, diarrhea, and nausea, which occur from 30 minutes to two hours after eating a lactose-containing food.

4. I have performed, or have had performed under my supervision, studies evaluating the effectiveness of a composition containing *Bacillus coagulans* bacteria (400 million colony forming units per dose) and a supplementary lactase (3000 units per dose), prepared under the brand name "Digestive Advantage."

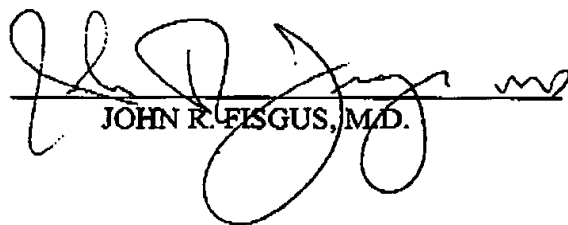
5. In a qualitative study involving fifteen human patients, the effectiveness of Digestive Advantage in reducing lactose intolerance, was compared with (a) a lactase enzyme product (such as Lactaid™) alone and (b) with no treatment. Symptoms of lactose intolerance (e.g., abdominal pain, cramping, diarrhea, bloating, gas and nausea) were evaluated in a questionnaire format following treatment with Digestive Advantage (mean period of use: 13.5 days). Patients rated the severity of their symptoms on a scale of 0-5, where 0 = no symptoms, 1 = minimal, 2 = mild, 3 = moderate, 4 = moderately severe, and 5 = very severe. Results of the study are shown in attached Appendix A.

6. The results of the study show that a composition containing *Bacillus coagulans* bacteria (400 million colony forming units per dose) and a supplementary lactase (3000 units per dose) was more effective than a lactase enzyme product alone in reducing the symptoms of lactose intolerance. Digestive Advantage reduced abdominal pain by 80.3%, as compared to a 3.3% reduction by lactase enzyme treatment alone. Similarly, Digestive Advantage reduced cramping by 80.3%, as compared to a 25.6% reduction by lactase enzyme treatment alone. Further, lactase enzyme treatment alone increased nausea by 15.6%, while use of Digestive Advantage decreased nausea by 81.8%.

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7. The results of the study indicated that a combination of *Bacillus coagulans* bacteria and a supplementary lactase led to an unexpected increase in bioavailability of nutrients as measured by a reduction of symptoms of lactose intolerance.

8. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001, Title 18, United States Code, and that willful false statements may jeopardize the validity of this application and any patent issuing therefrom.



JOHN R. EISGUS, M.D.

Signed at Cleveland, OH  
this 2 day of April

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**APPENDIX A**

Symptom	No treatment	lactase enzyme alone		Digestive Advantage	
	Mean severity of symptom	Mean severity of symptom	$\Delta$ vs. no treatment	Mean severity of symptom	$\Delta$ vs. no treatment
Abdominal Pain	2.69	2.60	- 3.3%	0.53	- 80.3%
Cramping	2.54	1.89	- 25.6%	0.50	- 80.3%
Diarrhea	2.77	1.89	- 31.8%	0.57	- 79.4%
Bloating	3.00	2.22	- 22.0%	0.71	- 76.3%
Gas	3.77	3.00	- 20.4%	1.96	- 48.0%
Nausea	0.77	0.89	+ 15.6%	0.14	- 81.8%

0 = no symptoms, 1 = minimal, 2 = mild, 3 = moderate, 4 = moderately severe, and 5 = very severe.

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